

REMARKS

I. Status of the Claims

Claims 8, 9 and 12-15 remain pending. Claim 8 has been amended to more clearly place the period at the end of the claim. New claims 16-18 have been added. Support for those claims is found throughout the specification and original claims. For example, support for claims 16 and 17 is found in original claims 8, 9, and 12-14, in the specification in the paragraph that bridges pages 34 and 35, on pages 14-15 in the Description of Figure 1, and in Figure 1. Support for claim 18 is found in claim 15, and in the specification at least in the paragraph that bridges pages 34 and 35. The amendment adds no new matter.

II. Information Disclosure Statement

Applicants note with appreciation that the Office has considered the Information Disclosure Statement filed April 9, 2004. However, the Office did not consider Sarver et al., "Ribozymes as Potential Anti-HIV-1 Therapeutic Agents," Science, 247: 1222-1225 (1990), because a copy of the article was not available to the Examiner. Applicants include as part of this response another copy of the article. Applicants respectfully request the Office consider the article and provide an initialed copy of page 4 of the Form PTO-1449 with the next Office Action.

III. Claims 8, 9, and 12-15 Are Definite

The Office rejects claims 8, 9, and 12-15 under 35 U.S.C. § 112, second paragraph because, according to the Office, the claims are indefinite. Office Action, page 2. Applicants respectfully traverse these rejections.

A. Counting from the 5' or 3' End

The Office finds it unclear whether the counting of the nucleotides referenced in the claims begins at the 5' or the 3' end and whether this numbering takes into account flanking sequences. Office Action, page 3. As the Office points out, it is conventional in the art to number nucleotide sequences by beginning at the 5' end and counting in the direction of the 3' end. See *id.* at 2. The Office states that the numbering in the instant claims is unclear, however, because "the nomenclature is not defined in the specification." *Id.*

According to the M.P.E.P., not only is the content of the disclosure used in determining whether a claim is definite, but the teachings of the prior art and the claim interpretation that would be given by one of ordinary skill in the art at the time the invention was made are also considered. M.P.E.P. § 2173.02, page 2100-205. Here, the specification discloses each sequence with the 5' and 3' ends clearly labeled. Starting at the 5' end of secondary structure (I), as recited in claim 8, and counting towards the 3' end, nucleotides 8-14 and 73-79 are those nucleotides shown to form hydrogen bonds in the amino acyl stem of the structure. See *also* Specification at page 4, lines 13-18. In addition, the Sequence Listing numbers the sequences in a 5' to 3' direction, so that nucleotides 8-14 and 73-79 of SEQ ID NO: 4 are clearly defined and their corresponding position in secondary structure (I) definite. Further, although the sequence presented in claim 8 is SEQ ID NO: 4, the claim is not drawn to SEQ ID NO: 4 *per se*. Instead, the claim is to "[a]n RNA variant adopting the following secondary structure (I)." Thus SEQ ID NO: 4 illustrates a secondary structure which is shared by all RNA variants within the claimed genus.

Applicants respectfully submit that there is no ambiguity regarding the numbering of the nucleotides in claim 8 in view of the clearly labeled 5' and 3' ends. Applicants therefore request withdrawal of the rejection.

B. Counting of Flanking Sequences

The Office also states that it is unclear whether flanking sequences are included in the counting of the nucleotides. Office Action, page 2. Applicants respectfully submit that the claims are clear that the numbering of the nucleotides is with reference to SEQ ID NO: 4, which illustrates secondary structure (I). For example, claim 8 recites that the RNA variant “comprises a bulge structure *introduced* in the region in which hydrogen bonds form between nucleotides 8 to 14 and nucleotides 73 to 79.” Emphasis added. The counting of the nucleotides simply indicates in which region of the structure the bulge is formed. Claim 9 recites that the bulge structure is introduced by substituting all or part of the sequence of the region of nucleotides 73 to 79. Because the claims encompass RNA variants comprising bulge structures of various sizes, introduced into RNA variants of various sequences, Applicants respectfully submit that this claim language is as clear as the subject matter permits, which is all the law requires. See M.P.E.P. § 2173.02, page 2100-205; *Orthokinetics, Inc. v. Safety Travel Chairs, Inc.*, 806 F.2d 1565, 1 USPQ2d 1081 (Fed. Cir. 1986). Applicants request the Office withdraw this rejection.

C. “Linked”

In its rejection of the claims as allegedly being indefinite, the Office also states that it is unclear what is meant by the term “linked” in claims 12, 13, and 14. Office

Action, page 3. According to the Office, the specification “does not teach what type of linkage is to be used or where the linkage is located.” *Id.* Further, claim 14 is rejected because, according to the Office, “[i]t is unclear whether any nucleotide of the RNA chain is linked to the 3’ terminus of SEQ ID NO: 4 or the 3’ terminus of itself, or of another structure.” *Id.*

Applicants respectfully submit that there is no need to further describe the nature of the linkage recited in claims 12-14. The specification provides examples in which the RNAs are linked covalently by virtue of transcription from a DNA sequence. *See, e.g.,* Specification at pages 34-35 (“Design of expression cassettes”). Moreover, as the Office notes, other methods of linking ribozymes via non-covalent bonds were also known in the art. *See* Office Action, page 5. Neither is it necessary to specify whether the selected RNA is added to the 5’ or the 3’ end. “Breadth of a claim is not to be equated with indefiniteness.” M.P.E.P §2173.04, page 2100-207 (citing *In re Miller*, 441 F.2d 689, 169 USPQ 597 (CCPA 1971)). Merely because the claims encompass more than one type of linkage, this does not mean that the claim is indefinite. If that were the case, any claim that recited a genus would be unpatentable for indefiniteness.

Further, Applicants respectfully submit that claim 14 is unambiguous. That claim recites specific details regarding how the bulge structure is formed. Taken in the context of claim 12, from which claim 14 depends, it is clear that there are two recited components that contribute to the formation of the bulge. The first recited component in claim 14 is an RNA chain, i.e, the “selected RNA chain linked thereto” of claim 12, that is linked to the 3’ terminus of the RNA variant. The second component is the region of nucleotides 8 to 14 within the nucleotide sequence of an RNA adopting secondary

structure (I), i.e., the RNA variant. Figure 1 illustrates this arrangement for several different structures. For example, Figure 1A shows an amino-acyl stem formed by hydrogen bonding between nucleotides contributed by the tRNA sequence, which is “the region of nucleotides 8 to 14 within the nucleotide sequence of an RNA adopting secondary structure (I),” and the ribozyme sequence, which is “an RNA chain linked to the 3’ terminus”. The bulge appears on the left hand side of the structure. Applicants respectfully submit that it is clear from the language of the claims that, in claim 14, the RNA chain is linked to the 3’ terminus of the RNA variant. Applicants therefore respectfully request the Office withdrawn the rejection.

IV. Claims 8, 9, and 12-15 Are Adequately Described

The Office also rejects claims 8, 9, and 12-15 under 35 U.S.C. § 112, first paragraph as failing to comply with the written description requirement. Office Action, page 3. With assertions similar to the ones made under the second paragraph of Section 112 above, the Office argues that the specification does not define how the nucleotides are to be counted, whether flanking sequences are included in the counting, and the type and location of the linkage between the RNA variant and the selected RNA chain, so that “one of ordinary skill in the art would not have been able to recognize what the claimed structure encompasses.” *Id.* at 4-6. In making those arguments, the Office points to references teaching that ribozymes can have flanking sequences, and a reference teaching that multiple linkages can be used to link ribozymes to various moieties. *Id.* at 5. Applicants respectfully traverse this rejection.

As discussed above, claim 8 is to “[a]n RNA variant adopting the following secondary structure (I).” SEQ ID NO: 4 in claim 8 illustrates a secondary structure

which is shared by all RNA variants within the claimed genus. The recitation of particular nucleotides in the claims identifies where within the reference structure the bulge is formed, i.e., within the amino-acyl stem. Neither does it matter whether any ribozyme linked to the RNA variant has flanking sequence because the nucleotide numbering is only in relationship to secondary structure (I), which is modified to produce the RNA variant to which the selected RNA is linked.

Likewise, there is no requirement that Applicants identify exactly which linker is used or at what location the linker is placed. The claims recite a core structure, secondary structure (I), which is modified by the introduction of a bulge structure in the amino-acyl stem to form the RNA variant recited in claims 8 and 9. Claims 12-14 recite an RNA molecule comprising the RNA variant linked to another RNA of interest. As the Office acknowledges, at the time the invention was made, methods of linking various ribozymes, i.e., RNA sequences of interest, to other moieties were known. "Information which is well known in the art need not be described in detail in the specification."

M.P.E.P. § 2163.II.A.2, page 2100-170 (citing *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 137980, 231 USPQ 81, 90 (Fed. Cir. 1986)). Further, the specification provides working examples which include three different linker sequences. See, e.g., Figures 1A-1C and accompanying text. The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species. M.P.E.P. § 2163.05, page 2100-180. The disclosed species, particular when viewed in conjunction with the knowledge in the art, provide more than an adequate description of the linkers used to attach a selected RNA chain to an RNA variant having secondary structure (I).

Applicants respectfully submit that the skilled artisan would have readily appreciated that Applicants were in possession of the claimed invention as a whole at the time the application was filed. The rejection should therefore be withdrawn.

V. Conclusion

In view of the foregoing amendments and remarks, Applicants respectfully request reconsideration and reexamination of this application and the timely allowance of the pending claims.

Please grant any extensions of time required to enter this response and charge any additional required fees to our Deposit Account No. 06-0916.

Respectfully submitted,

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